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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/030,566	01/07/2002	George von Samson-Himmelstjerna	Mo-6878/LeA 33,759	8763

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EXAMINER	
SITTON, JEHANNE SOUAYA	
ART UNIT	**PAPER NUMBER**
1634	

SHORTENED STATUTORY PERIOD OF RESPONSE	MAIL DATE	DELIVERY MODE
3 MONTHS	02/08/2007	PAPER

Please find below and/or attached an Office communication concerning this application or proceeding.

If NO period for reply is specified above, the maximum statutory period will apply and will expire 6 MONTHS from the mailing date of this communication.

Office Action Summary	Application No.	Applicant(s)	
	10/030,566	SAMSON-HIMMELSTJERNA ET AL.	
	Examiner	Art Unit	
	Jehanne S. Sitton	1634	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *31 October 2006*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-28,30-38 and 40-46* is/are pending in the application.

4a) Of the above claim(s) *5-10,12,20-27,30,31,35-38 and 40-46* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-4,11,13-19,28 and 32-34* is/are rejected.

7)☒ Claim(s) *4,11,13-19,28 and 32* is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date *10/04, 2/04*.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application
6) ☒ Other: Alignment w/Seq ID NO: 1

DETAILED ACTION

Election/Restrictions

1. This office action is in response to the papers filed 10/6/2004 and 1/18/2006. Applicant's election with traverse of Group 1, SEQ ID NO: 1 (Cyathostomum coronatum), and SEQ ID NOS: 40, 42, 43, and 44 (for claims 32-34) in the replies filed on 10/6/2004 and 1/18/2006 is acknowledged. It is noted that SEQ ID NO: 1 corresponds to a sequence from Cyathostomum coronatum and therefore, claims 10 and 12, directed to sequences from Cylicocyclus, are withdrawn from consideration as being drawn to a non elected invention.

2. The reply filed 10/6/2004 traversed the rejection. The traversal was on the grounds that the claims have a special technical feature because the application as a whole is directed at an approach to identifying and destroying a virulent family of nematodes responsible for causing a great deal of harm. This is not found persuasive for the reasons made in the restriction requirement dated 7/1/2004 which specifically set forth the reasons for why a special technical feature was lacking. The response further asserted that it was unclear whether 35 USC 372(b)(2) requires the examiner to apply the PCT rules or the Section 121 restriction requirement rules. This is not found persuasive.

MPEP 801 states,

> "This chapter is limited to a discussion of the subject of restriction and double patenting under Title 35 of the United States Code and Title 37 of the Code of Federal Regulations as it relates to national applications filed under 35 U.S.C. 111(a). **The discussion of unity of invention under the Patent Cooperation Treaty Articles and Rules as it is applied as an International Searching Authority, International Preliminary Examining Authority, and in applications entering the National Stage under 35 U.S.C. 371 as a Designated or Elected Office in the U.S. Patent and Trademark Office is covered in Chapter 1800** (emphasis added)."

Referring to Chapter 1800, MPEP 1893.03(d) states,

The principles of unity of invention are used to determine the types of claimed subject matter and the combinations of claims to different categories of invention that are permitted to be included in a single international or national stage patent application. The basic principle is that an application should relate to only one invention or, if there is more than one invention, that applicant would have a right to include in a single application only those inventions which are so linked as to form a single general inventive concept. A group of inventions is considered linked to form a single general inventive concept where there is a technical relationship among the inventions that involves at least one common or corresponding special technical feature.

The response further traversed that there was no burden of search. This was not found persuasive for the reasons made of record in the office action dated 12/23/2004, page 3. The requirements are still deemed proper and therefore made FINAL.

Claims 1, 14-19, and 28 link(s) the inventions of SEQ ID NOS 1, 3, 5, 7, 9 and 11. The restriction requirement among the linked inventions is **subject to** the nonallowance of the linking claim(s). Upon the indication of allowability of the linking claim(s), the restriction requirement as to the linked inventions **shall** be withdrawn and any claim(s) depending from or otherwise requiring all the limitations of the allowable linking claim(s) will be rejoined and fully examined for patentability in accordance with 37 CFR 1.104. **Claims that require all the limitations of an allowable linking claim** will be entered as a matter of right if the amendment is presented prior to final rejection or allowance, whichever is earlier. Amendments submitted after final rejection are governed by 37 CFR 1.116; amendments submitted after allowance are governed by 37 CFR 1.312. Applicant(s) are advised that if any claim presented in a continuation or divisional application is anticipated by, or includes all the limitations of, the allowable linking claim, such claim may be subject to provisional statutory and/or nonstatutory double patenting rejections over the claims of the instant application. Where a restriction requirement is withdrawn, the provisions of 35 U.S.C. 121 are no longer applicable. *In re Ziegler*, 443 F.2d 1211, 1215, 170 USPQ 129, 131-32 (CCPA 1971). See also MPEP § 804.01.

3. Accordingly, claims 5-9, 10, 12, 20-27, 30-31, 35-38, and 40-46, as well as SEQ ID NOS 2-39, 41, and 45-51 are withdrawn from consideration as being drawn to non elected inventions. Claims 29 and 39 are canceled. An office action on the merits of claims 1-4, 11, 13-19, 28 and 30-32 follows.

4. It is noted that the response filed 7/18/2006 provided a number of claim amendments, but that the claims do not accurately reflect amendments to the claims made in a preliminary amendment filed 1/26/2004. Accordingly, the claim set presented on 7/18/2006 is the most recent version of the claims and is under consideration at this time. Applicant is required to properly designate all claim amendments in any subsequent amendment. Failure to do so will cause the amendment to be held non responsive.

Information Disclosure Statement

5. The information disclosure statement filed 10/14/2004 fails to comply with 37 CFR 1.98(a)(3) because it does not include a concise explanation of the relevance, as it is presently understood by the individual designated in 37 CFR 1.56(c) most knowledgeable about the content of the information, of each patent or reference listed that is not in the English language. These references (EP 015,473; EP 173,149; DE 3430683; and Ulrich D. et al; 1988, vol. 101, pages 406-408) have been placed in the application file, but the information referred to therein has not been considered.

Specification

6. The amendment filed 10/31/2006 is objected to under 35 U.S.C. 132(a) because it introduces new matter into the disclosure. 35 U.S.C. 132(a) states that no amendment shall introduce new matter into the disclosure of the invention. The added material which is not supported by the original disclosure is as follows: The sequence listing was amended to provide designations for certain "XAA" amino acid designations. The new sequence listing states that "XAA" is a variable amino acid (see for example SEQ ID NO: 4). Although this is recited at page 26 of the specification, this variation is cited specifically for certain variable nucleotide positions in SEQ ID NO: 3. The designation of SEQ ID NO: 4 to encompass any variable amino acid, however, broadens the sequence originally recited for SEQ ID NO: 4. For example, as shown at pages 65-67 of the original sequence listing, XAA is designated for each position to be a specific amino acid, or at most 2 or 3 possible amino acids. However, the newly filed sequence listing submitted 10/31/2006, now encompasses that these positions be "any" amino acid, which represents a broadening of the invention outside the scope of that which appears to have been contemplated at page 26 of the specification and the originally filed sequence listing.

Applicant is required to cancel the new matter in the reply to this Office Action.

Claim Objections

7. Claims 4, 11, 13-14, 16, 18 and 32 are objected to because of the following informalities: the claims either recite the term "claims" (plural) or lack an article or preposition rendering the claims grammatically incorrect. Appropriate correction is required.

8. Claims 15, 17, 19, 28, and 32 are objected to under 37 CFR 1.75(c) as being in improper form because a multiple dependent claims can refer to more than one claim in the alternative only. Additionally, a multiply dependent claim cannot depend from another multiply dependent claim. Normally, such claims would not be further treated on the merits, however, as applicants had provided an amendment to such claims dated 1/26/2004 (although it is not the most recent version of the claims) for the purposes of compact prosecution, the claims have been treated as if they were only dependent from claim 1. Appropriate correction is required.

Claim Rejections - 35 USC § 101

9. 35 U.S.C. 101 reads as follows:

> Whoever invents or discovers any new and useful process, machine, manufacture, or composition of matter, or any new and useful improvement thereof, may obtain a patent therefor, subject to the conditions and requirements of this title.

10. Claims 1-4, 11, 13-19 and 32 are rejected under 35 U.S.C. 101 because the claimed invention is directed to non-statutory subject matter. The claims do not distinguish over nucleic acids as they exist naturally because the claims do not particularly point out any non naturally occurring differences between the claimed products and naturally occurring ones. In the absence of the hand of man, the naturally occurring products are considered non statutory subject matter. See Diamond v. Chakrabarty, 447 U.S. 303, 206 USPQ 193 (1980). The claims should be amended to indicate the hand of the inventor, however applicants should take care not to enter new matter into the claimed invention.

Claim Rejections - 35 USC § 112

11. The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

12. Claims 1-4, 11, 13-19, 28, and 32-34 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for an isolated nucleic acid molecule comprising SEQ ID NO: 1 or encoding SEQ ID NO: 2, or consisting of SEQ ID NOS: 40, 42, 43, or 44, does not reasonably provide enablement for the nucleic acids, vectors, and host cells as set forth in the claims. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the invention commensurate in scope with these claims. There are many factors to be considered when determining whether there is sufficient evidence to support determination that a disclosure does not satisfy the enablement requirements and whether any necessary experimentation is undue. These factors have been described by the court in *In re Wands*, 8 USPQ2d 1400 (CA FC 1988). *Wands* states at page 1404,

> "Factors to be considered in determining whether a disclosure would require undue experimentation have been summarized by the board in Ex parte Forman. They include (1) the quantity of experimentation necessary, (2) the amount of direction or guidance presented, (3) the presence or absence of working examples, (4) the nature of the invention, (5) the state of the prior art, (6) the relative skill of those in the art, (7) the predictability or unpredictability of the art, and (8) the breadth of the claims."

The claims are drawn to nucleic acid sequences which encode B-tubulin from any species of Cyathostaminae or any species of Cyathostomum, as well as generally any sequence which originates from Cyathostomum coronatum, as well as sequences with 85% identity to any

sequence "set forth in" SEQ ID NO: 1, or with at least 95% identity to a polynucleotide encoding SEQ ID NO: 2, sequences comprising a sequence "as set forth in" SEQ ID NO: 1, sequences with any base replacement in codon 200 which causes the DNA sequence to express a polypeptide having anthelminitic resistance, DNA and RNA complementary sequence thereto, as well as sequences which hybridize to such sequences, and sequences which comprise SEQ ID NOS 40, 42, 43, or 44 or sequences "derived" from any of the sequences named above. The claims are additionally drawn to vectors, host cells, and expression constructs, comprising the nucleic acids in the claims.

The invention is in a class of inventions which the CAFC has characterized as 'the unpredictable arts such as chemistry and biology" (Mycolgen Plant Sci., Inc. v. Monsanto Co., 243 F.3d 1316, 1330 (Federal Circuit 2001)).

The claims encompass an extremely broad genus of possible nucleic acid molecules, which are not commensurate in scope with the teachings of the specification. The specification teaches that SEQ ID NO: 1 is a sequence encoding B-tubulin for Cyathostomum coronatum and SEQ ID NOS 3, 5, 7, 9, and 11 encode B-tubulin for Cylicocyclus nassatus. The specification teaches only a single variant, at codon 200 which is either a Phe or Tyr, but does not teach any other variants at that codon which causes a DNA sequence to express a polypeptide having anthelmintic resistance.

The recitation of "hybridizes specifically" does not provide sufficient structure/function correlation between the listed sequences and the sequences encompassed by the claims because the ability of a sequence to hybridize to another is based on its primary nucleotide sequence and is a structural, not functional limitation. Further, the recitation of "derived from" or a specific %

identity, does not provide any structure/function correlation between the listed sequence and sequences encompassed by the claims as they allow for a large number of possible variations in nucleotide structure. Even a single nucleotide change between two sequences would not affect hybridization between the two sequences in most cases, however such alteration could abolish the activity or function of the encoded protein. The claims therefore encompass an extremely large genus of mutants, variants, and homologs of SEQ ID NO 1. The recitation of "from Cyathostominae" as well as the genus Cyathostomum, or Cyathostomum coronatum, in claims 1, 11 and 13, does not provide for sufficient structural or functional descriptions of the encompassed nucleic acids, vectors and host cells to distinguish them from other sequences because the specification fails to provide guidance that would allow the skilled artisan to determine whether any particular nucleic acid sequence was from the recited subfamily, genus, or species, other than by a specific SEQ ID NO: . Firstly, the specification provides no guidance as to which organisms are encompassed by the recitation of the subfamily "Cyathostominae". This lack of guidance is not resolved by the teachings in the art as there appears to be disagreement as to which species are covered by this subfamily. For example, Hung (Hung et al; International Journal of Parasitology; vol. 30, 2000, pages 95-103) teaches an attempt to provide a framework for equine strongyles based on ribosomal sequence data and specifically teaches "the sequence data did not provide support for the currently accepted division of the subfamilies Strongylinae and Cyathostominae based on morphological characteristics" (page 101, col. 1, lines 10-13). Secondly, the genus Cyathostomum, encompass structurally distinct B-tubulin sequence from number of different species, including C. catinatum, C. labiatum, C. labratum, and C. paternatum, whereas the specification has only provided the sequence of C. coronatum

(SEQ ID NO: 1). As shown in the alignment below (section 13), there are a number of structural differences between sequences from this genus alone and SEQ ID NO: 1, however the specification does not teach or describe any of these structural differences.

Additionally, the specification teaches that B-tubulin sequences for Cyathostomum coronatum (SEQ ID NO: 1 and 2; nucleic acid and protein respectively) and Cylicocyclus nassatus (SEQ ID NOS 3-11) exhibit 95-99.8% identity to each other (page 4, lines 22-26), however the specification does not teach or provide any guidance as to how to distinguish these sequences for each species, other than by SEQ ID NO:.

Thus given the broad claims in an art whose nature is identified as unpredictable, the unpredictability of that art, the large quantity of research required to define these unpredictable variables, the lack of guidance provided in the specification, balanced only against the high skill level in the art, it is the position of the examiner that it would require undue experimentation for one of skill in the art to make and us the nucleic acids encompassed by the claim as broadly written.

13. Claims 1-4, 11, 13-19, 28, and 32-34 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention.

The claims are drawn to nucleic acid sequences which encode B-tubulin from any species of Cyathostaminae or any species of Cyathostomum, as well as generally any sequence which

originates from Cyathostomum coronatum, as well as sequences with 85% identity to any sequence "set forth in" SEQ ID NO: 1, or with at least 95% identity to a polynucleotide encoding SEQ ID NO: 2, sequences comprising a sequence "as set forth in" SEQ ID NO: 1, sequences with any base replacement in codon 200 which causes the DNA sequence to express a polypeptide having anthelminitic resistance, DNA and RNA complementary sequence thereto, as well as sequences which hybridize to such sequences, and sequences which comprise SEQ ID NOS 40, 42, 43, or 44 or sequences "derived" from any of the sequences named above. The recitation of % identity, complementary sequences, sequences "derived" from other sequences, as well as sequences which specifically hybridize to the DNA sequences listed in claims 1-4, 11, and 13-15 encompasses a very large variable genus of variants, mutants, and homologs of SEQ ID NO: 1.

In analyzing whether the written description requirement is met for a genus claim, it is first determined whether a representative number of species have been described by their complete structure. The recitation of "hybridizes specifically" does not provide sufficient structure/function correlation between the listed sequences and the sequences encompassed by the claims because the ability of a sequence to hybridize to another is based on its primary nucleotide sequence and is a structural, not functional limitation. Further, the recitation of "derived from" or a specific % identity, does not provide sufficient structure/function correlation between the listed sequence and sequences encompass by the claims as they allow for a large number of possible variations in nucleotide structure. Even a single nucleotide change between two sequences would not affect hybridization between the two sequences in most cases, however such alteration could abolish the activity or function of the encoded protein. The claims

therefore encompass an extremely large genus of mutants, variants, and homologs of SEQ ID NO 1. The recitation of "from Cyathostominae" as well as the genus Cyathostomum, or Cyathostomum coronatum, in claims 1, 11 and 13, does not provide for any structural or functional descriptions of the encompassed nucleic acids, vectors and host cells because the specification fails to teach any relevant identifying characteristics which would allow the skilled artisan to envision a sequence from the recited subfamily, genus, or species, other than the specific sequence of SEQ ID NO: 1. Firstly, the specification provides no guidance as to which organisms are encompassed by the recitation of the subfamily "Cyathostominae". This lack of guidance is not resolved by the teachings in the art as there appears to be disagreement as to which species are covered by this subfamily. For example, Hung (Hung et al; International Journal of Parasitology; vol. 30, 2000, pages 95-103) teaches an attempt to provide a framework for equine strongyles based on ribosomal sequence data and specifically teaches "the sequence data did not provide support for the currently accepted division of the subfamilies Strongylinae and Cyathostominae based on morphological characteristics" (page 101, col. 1, lines 10-13). Secondly, the genus Cyathostomum, encompass structurally distinct B-tubulin sequence from number of different species, including C. catinatum, C. labiatum, C. labratum, and C. paternatum, whereas the specification has only provided the sequence of C. coronatum (SEQ ID NO: 1). As shown in the alignment below, there are a number of structural differences between sequences from this genus alone and SEQ ID NO: 1, however the specification does not teach or describe any of these structural differences.

```
LOCUS       AF487833               1429 bp    mRNA    linear   INV 19-AUG-2002
DEFINITION  Cyathostomum pateratum beta-tubulin Cyp-1b mRNA, complete cds.
ACCESSION   AF487833
VERSION     AF487833.1  GI:22297082
```

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  Query Match           92.1%;  Score 1271.2;  DB 3;  Length 1429;
```

```
  Best Local Similarity   95.1%;  Pred. No. 0;
  Matches 1312;  Conservative    0;  Mismatches   68;  Indels    0;  Gaps    0;

Qy          1 ATGCGTGAGATCGTGCATGTACAAGCTGGACAATGTGGAAACCAAATTGGTTCCAAGTTT 60
              ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db         19 ATGCGTGAGATCGTGCATGTACAAGCTGGACAATGTGGAAACCAAATTGGTTCCAAGTTC 78

Qy         61 TGGGAAGTGATCTCTGACGAGCATGGCATTAAGCCCGATGGCACATACCACGGAGAATCT 120
              |||||||||||||||||  |||||  |||||||||||||||||||||||||  |||||||||
Db         79 TGGGAAGTGATCTCTGATGAGCACGGCATTAAGCCCGATGGCACATACCATGGAGAATCT 138

Qy        121 GATCTACAATTAGAACGAATCAATGTGTACTATAATGAAGCACATGGAGGCAAATATGTC 180
              ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db        139 GATCTACAATTAGAACGAATCAATGTGTACTATAATGAAGCACATGGAGGCAAATATGTT 198

Qy        181 CCACGTGCAGTTCTTGTTGATCTCGAGCCCGGAACTATGGATTCCGTCCGTTCCGGGCCA 240
              ||  |||||||||||||||||||||||||  ||||||||||  ||  ||||||||  ||||||
Db        199 CCCCGTGCAGTTCTTGTTGATCTCGAGCCTGGAACTATGGACTCAGTCCGTTCTGGGCCA 258

Qy        241 TACGGGCAATTGTTCCGCCCTGATAACTACGTGTTTGGACAGTCTGGCGCAGGAAATAAC 300
              ||  ||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db        259 TATGGGCAATTGTTCCGCCCTGATAACTACGTGTTTGGACAGTCTGGCGCAGGAAATAAC 318

Qy        301 TGGGCAAAAGGTCACTACACTGAAGGCGCTGAACTTGTCGACAATGTACTAGATGTAGTG 360
              ||||||||||||||||||||||||||||||||||||||||||||||||||  ||||||||||
Db        319 TGGGCAAAAGGTCACTACACTGAAGGCGCTGAACTTGTCGACAATGTATTAGATGTAGTG 378

Qy        361 CGAAAAGAAGCAGAAGGATGTGACTGTCTGCAGGGCTTCCAGCTAACTCACTCACTTGGA 420
              ||||||||||| ||||||||  ||  ||||||||||||||||||||||||||||||||||||
Db        379 CGAAAAGAAGCTGAAGGATGCGATTGTCTGCAGGGCTTCCAGCTAACTCACTCACTTGGA 438

Qy        421 GGAGGTACCGGTTCGGGTATGGGCACTCTCCTCATCTCCAAAATTCGGGAGGAGTATCCT 480
              ||||||||||| ||||||||||||||||||||||||||||||||||||||||||||||||||
Db        439 GGAGGTACCGGATCGGGTATGGGCACTCTCCTCATCTCCAAAATTCGGGAGGAGTATCCT 498

Qy        481 GATAGAATCATGTCCTCGTTCTCCGTTGTCCCCTCACCAAAGGTCTCCGACACTGTTGTG 540
              ||||||||||||||||||||||||||||| ||||||||||||||||  ||  |||||||||
Db        499 GATAGAATCATGTCCTCGTTCTCCGTTGTTCCCTCACCAAAGGTCTCTGATACTGTTGTG 558

Qy        541 GAGCCTTACAATGCTACCCTATCCGTTCATCAGTTGGTTGAAAATACAGACGAGACTTAT 600
              |||||  ||||||||||||||||||||||||||||||||||  ||||||||||  ||||
Db        559 GAGCCATACAATGCTACCCTATCCGTTCATCAGTTGGTTGAGAATACAGACGAAACTTTC 618

Qy        601 TGTATTGACAATGAAGCCCTGTATGATATTTGCTTCCGCACTTTGAAACTCACGAACCCA 660
              ||||||||||||||||  ||  ||||||||||||||||||  ||||||||||  ||||||
Db        619 TGTATTGACAATGAAGCTCTCTATGATATTTGCTTCCGCACCCTGAAACTCACAAACCCA 678

Qy        661 ACTTATGGAGATCTGAATCATCTTGTGTCTGTAACAATGTCTGGTGTCACCACATGTCTT 720
              ||||||||||||||||||||||||||||||||||  ||||||||||||||  |||||||||
Db        679 ACTTATGGAGATCTGAATCATCTTGTGTCTGTAACGATGTCTGGTGTCACTACATGTCTT 738

Qy        721 CGCTTCCCTGGCCAATTGAATGCCGATCTACGCAAACTAGCTGTTAACATGGTTCCATTC 780
              ||||||||||||||||||||||||||||||||  ||||||||||||||||||||||||||
Db        739 CGCTTCCCTGGCCAATTGAATGCCGATCTACGTAAACTAGCTGTTAACATGGTTCCATTC 798

Qy        781 CCTCGTCTTCACTTCTTCATGCCTGGTTTTGCTCCTCTTTCTGCTAAAGGTGCTCAGGCT 840
              ||||||||||||||||||||||||||  ||||||||  |||||  ||  |||||  |||||||||
Db        799 CCTCGTCTTCACTTCTTCATGCCTGGATTTGCTCCCCTTTCCGCCAAAGGCGCTCAGGCT 858

Qy        841 TACCGTGCTCTTACCGTAGCCGAGCTTACACAGCAGATGTTTGATGCTAAGAATATGATG 900
              |||||||||||||  ||||||||  |||||  ||||||||||  |||||  ||  |||||||||
Db        859 TACCGTGCTCTTACTGTAGCCGAACTTACCCAGCAGATGTTCGATGCCAAAAATATGATG 918

Qy        901 GCTGCTTGCGACCCTCGACATGGACGTTATCTCACCGTCGCAGCCATGTTCCGAGGAAGA 960
              ||||||||||| ||  ||||||||||||||||||||||  ||||||||||||||||  ||
Db        919 GCTGCTTGCGATCCGCGACATGGACGTTATCTCACCGTTGCAGCCATGTTCCGAGGACGA 978
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Qy        961 ATGAGCATGAGGGAAGTAGACGACCAGATGATGTCAGTGCAGAACAAGAACTCCTCATAC 1020
              ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db        979 ATGAGCATGAGGGAAGTAGACGACCAGATGATGTCAGTGCAGAACAAGAACTCCTCATAC 1038

Qy       1021 TTCGTAGAGTGGATCCCGAACAACGTGAAGACCGCTGTATGCGACATCCCGCCACGAGGA 1080
              |||||||||||||||||||||||| |||||||||||||||||| |||||| |||||
Db       1039 TTCGTAGAGTGGATCCCGAACAACGTCAAGACCGCTGTATGCGACATTCCGCCAAGAGGA 1098

Qy       1081 CTGAAGATGGCCGCTACCTTCGTTGGAAACTCAACTGCCATCCAAGAGCTGTTCAAGCGC 1140
              || || ||||||||||||| |||||||||| |||||||||||||||||||||||||||
Db       1099 CTAAAAATGGCCGCTACCTTTGTTGGAAACTCTACTGCCATCCAAGAGCTGTTCAAGCGC 1158

Qy       1141 ATTTCAGAACAATTTACAGCCATGTTCCGCCGCAAAGCGTTCTTGCATTGGTACACTGGT 1200
              ||||| |||||||| |||||||||||||||||||||||||||||||||||||||||||||
Db       1159 ATTTCGGAACAATTCACAGCTATGTTCCGCCGCAAAGCGTTCTTGCATTGGTACACTGGT 1218

Qy       1201 GAAGGTATGGACGAGATGGAGTTCACTGAAGCAGAGTCCAACATGAATGATCTCATCTCC 1260
              |||||||||| |||||||||||||||||||| || ||||||||||||||||||||||||
Db       1219 GAAGGTATGGATGAGATGGAGTTCACTGAAGCCGAATCCAACATGAATGATCTCATCTCC 1278

Qy       1261 GAGTACCAACAGTACCAGGAAGCCACCGCTGACGACATGGGCGATCTTGATGCGGAAGGC 1320
              |||||||||| |||||||||| |||||||||| |||||||||| ||||||||||
Db       1279 GAGTACCAACAATACCAGGAAGCTACCGCTGACGATATGGGCGATCTCGATGCGGAAGGC 1338

Qy       1321 GCTGAAGAGGCTTATCCTGAGGAATAAACCAGCAGATCGTGTTGCGTTGTTCGTTTCTCT 1380
              |||||||||| |||||||||||||| |||||||||||||||||||||||||  ||||||
Db       1339 GCTGAAGAGGCCTATCCTGAGGAATAGACCAGCAGATCGTGTTGCGTTGTTCAGTTCTCT 1398
```

Additionally, the specification teaches that B-tubulin sequences for Cyathostomum coronatum (SEQ ID NO: 1 and 2; nucleic acid and protein respectively) and Cylicocyclus nassatus (SEQ ID NOS 3-11) exhibit 95-99.8% identity to each other (page 4, lines 22-26), however the specification does not teach or provide any guidance as to how to distinguish these sequences for each species, other than by SEQ ID NO: 1.

Further, with regard to claims which encompass sequences comprising oligonucleotides such as, for example, SEQ ID NO: 43, the claims encompass the beta tubulin sequence from other undisclosed organisms such as Cyathostomum pateratum.

```
DEFINITION  Cyathostomum pateratum beta-tubulin Cyp-1a mRNA, complete cds.
ACCESSION   AF487832
VERSION     AF487832.1  GI:22297080
KEYWORDS    .
SOURCE      Cyathostomum pateratum
  ORGANISM  Cyathostomum pateratum


  Query Match             100.0%;  Score 22;  DB 13;  Length 1429;
  Best Local Similarity   100.0%;  Pred. No. 59;
  Matches   22;  Conservative    0;  Mismatches    0;  Indels    0;  Gaps    0;

Qy          1 CAAGCTGGACAATGTGGAAACC 22
```

```
                    ||||||||||||||||||||||
Db          40 CAAGCTGGACAATGTGGAAACC 61
```

As noted above, the genus encompassed by the broadly claimed invention encompass a large variable genus of mutants, variants and homologs of SEQ ID NO: 1, for which only a few species have been taught. SEQ ID NO: 1 is taught to be a sequence encoding B-tubulin for Cyathostomum coronatum and SEQ ID NOS 3, 5, 7, 9, and 11 are taught to encode B-tubulin for Cylicocyclus nassatus. The specification teaches only a single variant, at codon 200 which is either a Phe or Tyr, but does not teach any other variants at that codon which causes a DNA sequence to express a polypeptide having anthelmintic resistance. The specification provides no guidance as to how the structural difference between Phe and Tyr provides for anthelmintic resistance for the skilled artisan to be able to determine which other variants would have the same activity.

Accordingly, the specification has not adequately disclosed the relevant identifying characteristic of a representative number of species within the claimed genus.

Vas-Cath Inc. v. Mahurkar, 19 USPQ2d 1111, makes clear that "applicant must convey with reasonable clarity to those skilled in the art that, as of the filing date sought, he or she was in possession of the invention. The invention is, for purposes of the 'written description' inquiry, whatever is now claimed." (See page 1117.) The specification does not "clearly allow persons of ordinary skill in the art to recognize that [he or she] invented what is claimed." (See Vas-Cath at page 1116.)

With the exception of SEQ ID NOS: 1, 2, 40, and 42-44, the skilled artisan cannot envision the detailed chemical structure of the encompassed polynucleotides and/or proteins, regardless of the complexity or simplicity of the method of isolation. Adequate written

description requires more than a mere statement that it is part of the invention and reference to a potential method for isolating it. The nucleic acid itself is required. See Fiers v. Revel, 25 USPQ2d 1601, 1606 (CAFC 1993), and Amgen Inc. V. Chugai Pharmaceutical Co. Ltd., 18 USPQ2d 1016. In Fiddes v. Baird, 30 USPQ2d 1481, 1483, claims directed to mammalian FGF's were found unpatentable due to lack of written description for the broad class. The specification provided only the bovine sequence.

Finally, University of California v. Eli Lilly and Co., 43 USPQ2d 1398, 1404, 1405 held that:

> To fulfill the written description requirement, a patent specification must describe an invention and do so in sufficient detail that one skilled in the art can clearly conclude that "the inventor invented the claimed invention." Lockwood v. American Airlines, Inc., 107 F.3d 1565, 1572, 41 USPQ2d 1961, 1966 (1997); In re Gosteli, 872 F.2d 1008, 1012, 10 USPQ2d 1614, 1618 (Fed. Cir. 1989) (" [T]he description must clearly allow persons of ordinary skill in the art to recognize that [the inventor] invented what is claimed."). Thus, an applicant complies with the written description requirement "by describing the invention, with all its claimed limitations, not that which makes it obvious," and by using "such descriptive means as words, structures, figures, diagrams, formulas, etc., that set forth the claimed invention." Lockwood, 107 F.3d at 1572, 41 USPQ2d at 1966.
>
> An adequate written description of a DNA, such as the cDNA of the recombinant plasmids and microorganisms of the '525 patent, "requires a precise definition, such as by structure, formula, chemical name, or physical properties," not a mere wish or plan for obtaining the claimed chemical invention. Fiers v. Revel, 984 F.2d 1164, 1171, 25 USPQ2d 1601, 1606 (Fed. Cir. 1993). Accordingly, "an adequate written description of a DNA requires more than a mere statement that it is part of the invention and reference to a potential method for isolating it; what is required is a description of the DNA itself." Id. at 1170, 25 USPQ2d at 1606.

14. The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

15. Claims 1-4, 11, 13-19, 28, and 32-34 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Claim 1 recites that the sequence be "form Cyathostominae", however the specification provides no definition as to sequences which would be considered "from Cyathostominae" other than SEQ ID NOS 1, 3, 5, 7, 9, an 11. It is unclear if the claims are therefore limited to these sequences, or to any sequences from this subfamily. If the latter is the case, it is noted that the specification provides no clear description as to metes and bounds of this family, whereas there is disagreement in the art regarding species which may or may not belong in this subfamily (see Hung et al; cited above). Accordingly, the metes and bounds of the claims are unclear.

In claim 33, there is insufficient antecedent basis for the recitation of "oligonucleotides". The claim is dependent from claim 28, however claim 28 only recites a single oligonucleotide. Accordingly, it is unclear which additional oligonucleotides are being referred to in claim 33.

Claim Rejections - 35 USC § 102

16. The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
>
> (a) the invention was known or used by others in this country, or patented or described in a printed publication in this or a foreign country, before the invention thereof by the applicant for a patent.
>
> (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.
>
> (e) the invention was described in (1) an application for patent, published under section 122(b), by another filed in the United States before the invention by the applicant for patent or (2) a patent granted on an application for patent by another filed in the United States before the invention by the applicant for patent, except that an international application filed under the treaty defined in section 351(a) shall have the effects for purposes of this subsection of an application filed in the United States only if the international application designated the United States and was published under Article 21(2) of such treaty in the English language.

17. Claims 1-4, 11, 13-15, 28 and 32-34 are rejected under 35 U.S.C. 102(b) as being anticipated by Brennan (US Patent 5,474,796).

The claims encompass an extremely large genus of possible oligomers. Brennan teaches an array of every possible 10 mer nucleic acid (see cols 9 and 10), which anticipate the claimed recitation of "fragments", "derived" from, "complementary" (this term is not limited to complementary over the full length of a molecule, eg: SEQ ID NO: 1), "set forth in", "a sequence", "hybridizes specifically", etc.

18. Claims 1-4, 11, 13-15, 17-19, 28, and 32-34 are rejected under 35 U.S.C. 102(b) as being anticipated by Roos (WO 92/03549).

It is noted that absent a clear definition as to which species are encompassed by the recitation of "Cyathostominae", the claims have been broadly interpreted to encompass the B-tubulin sequences taught by Roos. Additionally, it is noted that the recitation of "from" or "originates from" is not given any patentable weight as this recitation does not clearly set forth any specific structural requirements for a nucleic acid sequence, and does not distinguish a molecule which was isolated from the indicated organism and later mutated to contain a different nucleic acid sequence. Further, it is noted that claims 2 and 3 do not require % identity over the full length of SEQ ID NO: 1 or 2. Additionally, the term "complementary" does not require complementarity over the full length of the molecule (this can be overcome by reciting "the complement" instead).

Roos teaches a nucleic acid sequence for B-tubulin from a nematode (figure 2). Roos teaches primers and probes (oligonucleotides) to such sequence (page 6), kits comprising such, as well as vectors and recombinant microorganisms (page 8, lines 31-35) comprising such sequences. The sequence of Roos comprises a sequence "set forth in" SEQ ID NO: 1, and SEQ

ID NO: 40 (see below), and is further broadly interpreted as a sequence "derived" from the sequence in any of claims 1-15.

```
AAQ22665 standard; DNA; 1551 BP.
XX
AC   AAQ22665;
XX
DT   25-MAR-2003  (revised)
DT   23-JUL-1992  (first entry)
XX
DE   Sequence of beta-tubulin gene with introns.
XX
KW   Worm infection; diagnosis; PCR primer; alpha-tubulin; beta-tubulin; ss.
XX
OS   Haemonchus contortus.

PN   WO9203549-A.
XX
PD   05-MAR-1992.
XX
PF   15-AUG-1991;   91WO-N0000153.
XX
PR   16-AUG-1990;   90NL-00001832.
PI   Roos MH;


Qy          1 AACGCAATCAATGTGTATTTCGC 23
              ||||||| ||||||||||||||||
Db       1526 AACGCAACCAATGTGTATTTCGC 1504
```

19. Claims 1-4, 11, 13-19, 28 and 32 are rejected under 35 U.S.C. 102(b) as being anticipated by Elard (Elard et al; Molecular and Biochemical Parasitology, vol. 79, 1996, pages 249-253).

It is noted that absent a clear definition as to which species are encompassed by the recitation of "Cyathostominae", the claims have been broadly interpreted to encompass the B-tubulin sequences taught by Elard. Additionally, it is noted that the recitation of "from" or "originates from" is not given any patentable weight as this recitation does not clearly set forth any specific structural requirements for a nucleic acid sequence, and does not distinguish a molecule which was isolated from the indicated organism and later mutated to contain a different nucleic acid sequence. Further, it is noted that claims 2 and 3 do not require % identity over the

full length of SEQ ID NO: 1 or 2. Additionally, the term "complementary" does not require complementarity over the full length of the molecule (this can be overcome by reciting "the complement" instead).

Elard teaches a nucleic acid sequence for B-tubulin from a nematode (alignment provided) which possess a base at codon 200 responsible for anthelmintic resistance (see page 252, col. 1). Elard teaches oligonucleotides to such sequence. The recitation of "vectors", "host cell' and "expression construct" is considered an inherent property of the teachings of Elard. Elard further teaches constructing RNA (page 250, col. 2) and cDNA. The sequence of Elard comprises a sequence "set forth in" SEQ ID NO: 1, and SEQ ID NOS: 40 and 42-44 and is further broadly interpreted as a sequence "derived" from the sequence in any of claims 1-15.

Claim Rejections - 35 USC § 103

20. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

21. This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later

invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(e), (f) or (g) prior art under 35 U.S.C. 103(a).

22. Claims 33 and 34 are rejected under 35 U.S.C. 103(a) as being unpatentable over Elard in view of Roos.

Elard teaches a nucleic acid sequence for B-tubulin from a nematode (alignment provided) which possess a base at codon 200 responsible for anthelmintic resistance (see page 252, col. 1). Elard teaches oligonucleotides to such sequence. The recitation of "vectors", "host cell' and "expression construct" is considered an inherent property of the teachings of Elard. Elard further teaches constructing RNA (page 250, col. 2) and cDNA. The sequence of Elard comprises a sequence "set forth in" SEQ ID NO: 1, and SEQ ID NOS: 40 and 42-44 and is further broadly interpreted as a sequence "derived" from the sequence in any of claims 1-15. Elard does not teach packaging such nucleic acids in kit format, however Roos teaches kits comprising B-tubulin nucleic acids. Therefore, it would have been prima facie obvious to one of ordinary skill in the art at the time the invention was made to package the sequences of Elard in kit format, as taught by Roos, for the purpose of providing prepackaged reagents which would save a researcher time.

Conclusion

23. No claims are allowed. A nucleotide molecule comprising SEQ ID NO: 1 is free of the prior art.

24. Any inquiry concerning this communication or earlier communications from the examiner should be directed to examiner Jehanne Sitton whose telephone number is (571) 272-

0752. The examiner can normally be reached Monday-Thursday from 8:00 AM to 5:00 PM and on alternate Fridays.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Ram Shukla, can be reached on (571) 272-0735. The fax phone number for this Group is (571) 273-8300.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to (571) 272-0547.

Patent applicants with problems or questions regarding electronic images that can be viewed in the Patent Application Information Retrieval system (PAIR) can now contact the USPTO's Patent Electronic Business Center (Patent EBC) for assistance. Representatives are available to answer your questions daily from 6 am to midnight (EST). The toll free number is (866) 217-9197. When calling please have your application serial or patent number, the type of document you are having an image problem with, the number of pages and the specific nature of the problem. The Patent Electronic Business Center will notify applicants of the resolution of the problem within 5-7 business days. Applicants can also check PAIR to confirm that the problem has been corrected. The USPTO's Patent Electronic Business Center is a complete service center supporting all patent business on the Internet. The USPTO's PAIR system provides Internet-based access to patent application status and history information. It also enables applicants to view the scanned images of their own application file folder(s) as well as general patent information available to the public.

For all other customer support, please call the USPTO Call Center (UCC) at 800-786-9199.

Jehanne Sitton
Primary Examiner
Art Unit 1634
2/2/07

Alignment w/ Seq ID NO: 1

```
RESULT 31
TCBTUBMRN
LOCUS       TCBTUBMRN               1460 bp    mRNA    linear   INV 06-AUG-1996
DEFINITION  T.circumcincta mRNA for beta-tubulin.
ACCESSION   Z69258
VERSION     Z69258.1  GI:1217657
KEYWORDS    beta-tubulin.
SOURCE      Teladorsagia circumcincta
  ORGANISM  Teladorsagia circumcincta
            Eukaryota; Metazoa; Nematoda; Chromadorea; Rhabditida; Strongylida;
            Trichostrongyloidea; Haemonchidae; Ostertagiinae; Teladorsagia.
REFERENCE   1  (bases 1 to 1460)
  AUTHORS   Elard,L., Comes,A.M. and Humbert,J.F.
  TITLE     Sequences of beta-tubulin cDNA from benzimidazole-susceptible and
            -resistant strains of Teladorsagia circumcincta, a nematode
            parasite of small ruminants
  JOURNAL   Mol. Biochem. Parasitol. 79 (2), 249-253 (1996)
  MEDLINE   97008419
   PUBMED   8855563
REFERENCE   2  (bases 1 to 1460)
  AUTHORS   Humbert,J.
  TITLE     Direct Submission
  JOURNAL   Submitted (31-JAN-1996) Humbert j., INRA, Station de Pathologie
            Aviaire, Nouzilly, FRANCE, 37380
COMMENT     On Mar 7, 1996 this sequence version replaced gi:1177365.
FEATURES             Location/Qualifiers
     source          1. .1460
                     /organism="Teladorsagia circumcincta"
                     /mol_type="mRNA"
                     /strain="benzimidazole-susceptible strain"
                     /db_xref="taxon:45464"
                     /tissue_type="whole organism"
                     /dev_stage="adult"
     CDS             41. .1387
                     /codon_start=1
                     /product="beta-tubulin"
                     /protein_id="CAA93249.1"
                     /db_xref="GI:1217658"
                     /db_xref="GOA:Q26901"
                     /db_xref="TrEMBL:Q26901"
                     /translation="MREIVHVQAGQCGNQIGSKFWEVISDEHGIQPDGTYKGESALQL
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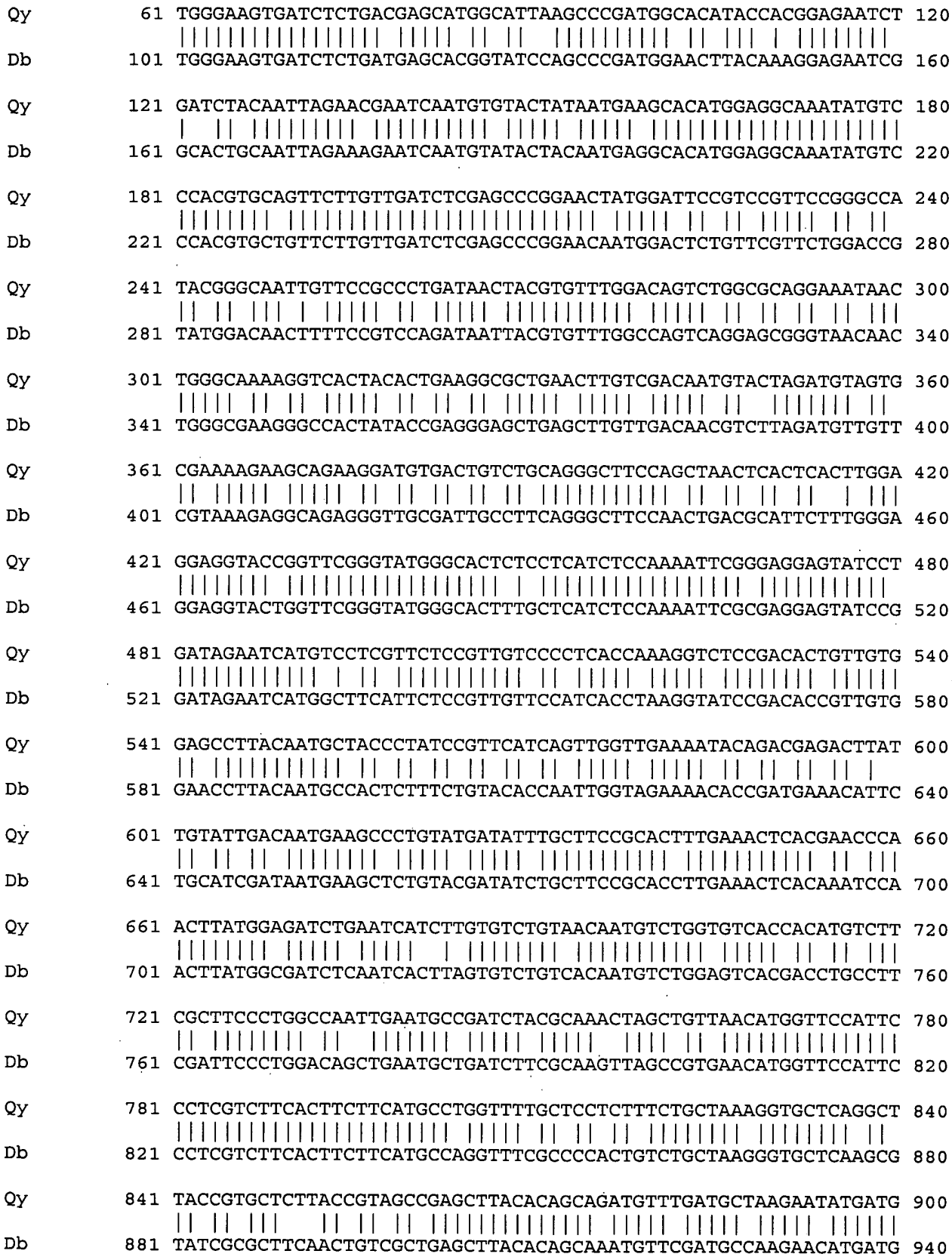
                     KGHYTEGAELVDNVLDVVRKEAEGCDCLQGFQLTHSLGGGTGSGMGTLLISKIREEYP
                     DRIMASFSVVPSPKVSDTVVEPYNATLSVHQLVENTDETFCIDNEALYDICFRTLKLT
                     NPTYGDLNHLVSVTMSGVTTCLRFPGQLNADLRKLAVNMVPFPRLHFFMPGFAPLSAK
                     GAQAYRASTVAELTQQMFDAKNMMAACDPRHGRYLTVAAMFRGRMSMREVDDQMMSVQ
                     NKNSSYFVEWIPNNVKTAVCDIPPRGLKMAATFVGNSTAIQELFKRISEQFTAMFRRK
                     AFLHWYTGEGMDEMEFTEAESNMNDLISEYQQYQEATADDMGDLDAEGAEEPYPEE"
ORIGIN

  Query Match             72.0%;  Score 993.4;  DB 3;  Length 1460;
  Best Local Similarity   82.8%;  Pred. No. 7.8e-281;
  Matches 1135;  Conservative    0;  Mismatches  236;  Indels    0;  Gaps    0;

Qy          1 ATGCGTGAGATCGTGCATGTACAAGCTGGACAATGTGGAAACCAAATTGGTTCCAAGTTT 60
              |||||||| ||||| |||||||||| || ||||| || ||||| || || || |||||
Db         41 ATGCGTGAAATCGTTCATGTACAAGCCGGTCAATGCGGTAACCAGATCGGATCAAAGTTC 100
```



```
Qy        901 GCTGCTTGCGACCCTCGACATGGACGTTATCTCACCGTCGCAGCCATGTTCCGAGGAAGA 960
              |||||||| || ||||| || ||||| ||||| || || || |||||||||||| ||  |
Db        941 GCTGCTTGTGATCCTCGCCACGGACGCTATCTGACGGTGGCGGCCATGTTCCGTGGTCGC 1000

Qy        961 ATGAGCATGAGGGAAGTAGACGACCAGATGATGTCAGTGCAGAACAAGAACTCCTCATAC 1020
              ||||||||| ||||||| |||||||| |||||||| |||||||||||||||| ||||||
Db       1001 ATGAGCATGCGGGAAGTGGACGACCAAATGATGTCCGTGCAGAACAAGAACTCGTCATAC 1060

Qy       1021 TTCGTAGAGTGGATCCCGAACAACGTGAAGACCGCTGTATGCGACATCCCGCCACGAGGA 1080
              ||||| || ||||| || |||||||| || |||||||| || ||||| || || || |||
Db       1061 TTCGTGGAATGGATTCCAAACAACGTAAAAACCGCTGTTTGTGACATTCCTCCTCGTGGA 1120

Qy       1081 CTGAAGATGGCCGCTACCTTCGTTGGAAACTCAACTGCCATCCAAGAGCTGTTCAAGCGC 1140
               |||| ||||| |||||||| ||||| ||||||||||||||||||||||||||||||||
Db       1121 TTGAAAATGGCTGCTACCTTTGTTGGTAACTCAACTGCCATCCAAGAGCTGTTCAAGCGT 1180

Qy       1141 ATTTCAGAACAATTTACAGCCATGTTCCGCCGCAAAGCGTTCTTGCATTGGTACACTGGT 1200
              ||||| || || || ||||| |||||||| ||||| || ||| | ||||||||||||||
Db       1181 ATTTCGGAGCAGTTCACAGCTATGTTCCGGCGCAAGGCTTTCCTCCATTGGTACACTGGT 1240

Qy       1201 GAAGGTATGGACGAGATGGAGTTCACTGAAGCAGAGTCCAACATGAATGATCTCATCTCC 1260
              || |||||||||||| ||||| ||||| ||||| ||||| |||||||||||||| |||||
Db       1241 GAGGGTATGGACGAAATGGAATTCACAGAAGCTGAGTCGAACATGAATGATCTTATCTCT 1300

Qy       1261 GAGTACCAACAGTACCAGGAAGCCACCGCTGACGACATGGGCGATCTTGATGCGGAAGGC 1320
              |||||||||||||||||| |||||||||||| |||||||||| ||||| |||||
Db       1301 GAGTACCAACAGTACCAGGAGGCCACCGCTGACGATATGGGCGATCTCGATGCAGAAGGT 1360

Qy       1321 GCTGAAGAGGCTTATCCTGAGGAATAAACCAGCAGATCGTGTTGCGTTGTT 1371
              || |||||| | || || ||||| |||     ||    ||   ||  | ||
Db       1361 GCAGAAGAGCCGTACCCCGAGGAGTAATGATCCACCGTGTTGCGCTGTTTT 1411
```